

Figure 1a: Schematic of recombinant vector that encodes the human β APP-C100.

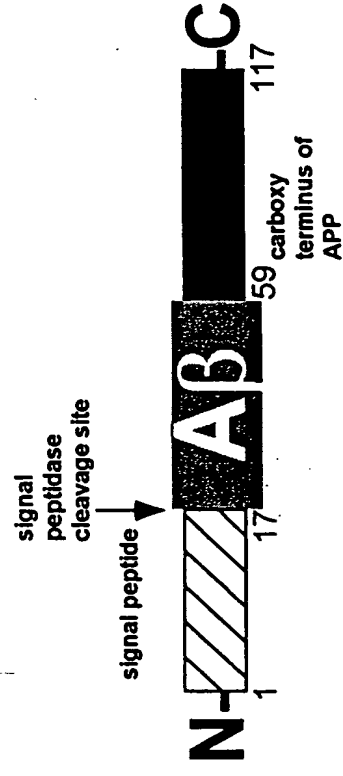


Figure 1b: Schematic of the recombinant vector that encodes the human β APP-C83 polypeptide.

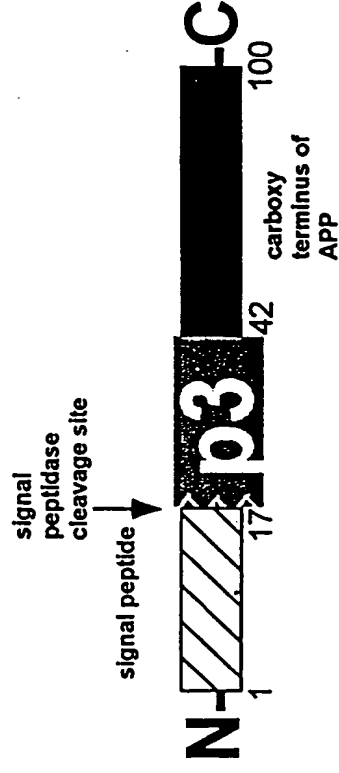


Figure 2: The nucleotide and amino acid sequence of the recombinant β APP (C-100) polypeptide substrate.

	10	30	50
	ATGCTGCCCGGTTTGGCACTGTTCCCTGCTGGCCGCTGGACGGCTCGGGCGCTGGATGCA		
1	M L P G L A L F L L A A W T A R A L D A	20	
	70	90	110
	GAATTCGACATGACTCAGGATATGAAGTTTCATCATCAAAAATTGGTGTCTTTCAGAA		
21	E F R H D S G Y E V H H Q K L V F F A E	40	
	130	150	170
	GATGTGGGTTCAAACAAGGTGCAATCATTTGGACTCATGGTGGCGGTGTGTATAGCG		
41	D V G S N K G A I I G L M V G G V I A	60	
	190	210	230
	ACAGTGATCGTCATCACCTTGGTGATGCTGAAGAAGAAACAGTACACATCCATTCATCAT		
61	T V I V I T L V M L K K K Q Y T S I H H	80	
	250	270	290
	GGTGTGGTGAGGTTGACGCGGCTGTCAACCCAGAGGAGCGCCACCTGTCCAAGATGCAG		
81	G V V E V D A A V T P E E R H L S K M Q	100	
	310	330	350
	CAGAACGGCTACGAAATCCAACCTACAAGTTCTTTGAGCAGATGCAGAACTAG		
101	Q N G Y E N P T Y K F F E Q M Q N *	118	

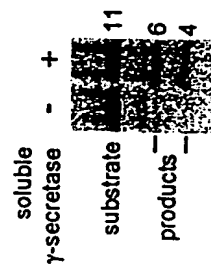
Figure 3: The nucleotide and amino acid sequence of the recombinant
 β APP (C-83) polypeptide substrate.

	10	30	50
	ATGCTGCCCGGTTTGGCACTGTTCTCTGCTGGCCGCTGGACGGCTCGGGCGCTGGATGCA		
1	M	L	P
	G	L	A
	L	F	L
	A	A	A
	W	T	A
	R	A	L
	D	A	
20			
	70	90	110
	GAATTCGTGTTCTTTGCAGAAGATGTGGGTTCAAAACAAGGTGCAATCATTTGGACTCATG		
21	E	F	V
	F	F	A
	E	D	V
	G	S	N
	K	G	A
	I	I	G
	L	M	
40			
	130	150	170
	GTGGCGGTGTTGTCATAGCGACAGTGCATGTCATCACCTTGGTGATGCTGAAGAAGAAA		
41	V	G	G
	V	I	A
	T	V	I
	V	I	V
	I	T	L
	V	M	L
	K	K	K
60			
	190	210	230
	CAGTACACATCCATTTCATGTTGTTGGTGGAGTTGACGCCGGTGTACCCCGAGAGGAG		
61	Q	Y	T
	S	I	H
	G	V	V
	E	V	D
	A	A	V
	T	P	E
80			
	250	270	290
	CGCCACCTGTCCAAGATGCAGCAGAACGGCTACGAAATCCAACCTACAAGTCTTTGAG		
81	R	H	L
	S	K	M
	Q	Q	N
	G	Y	E
	N	P	T
	Y	K	F
	F	E	
100			
	310		
	CAGATGCAGAACTAG		
101	Q	M	Q
	N	*	
105			

Figure 5: Putative gamma-secretase cleavage sequence within an S2-cleaved human Notch-1 fragment.

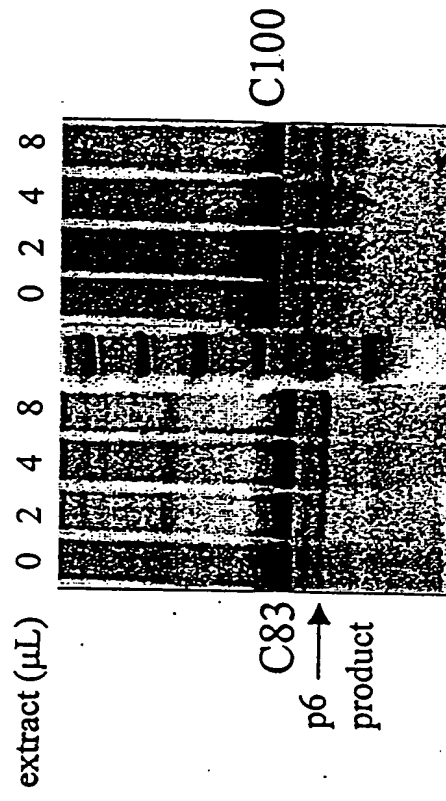
VQSETVEPPPPAQLHFMYYVAAAFVLLFFVGC[|]G[|]VLLSRKRR[|]

Figure 6: cleavage of 35S-C100 by soluble gamma
secretase preparation.



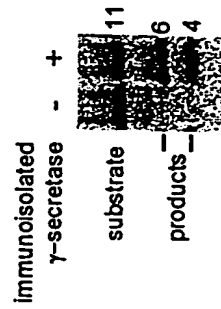
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Figure 7: cleavage of 35S-C83 and -C100 by soluble gamma secretase preparation.



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Figure 8: cleavage of 35S-C100 by immunoisolated
gamma secretase preparation



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Detection of γ -Secretase Cleavage in Isolated Membranes

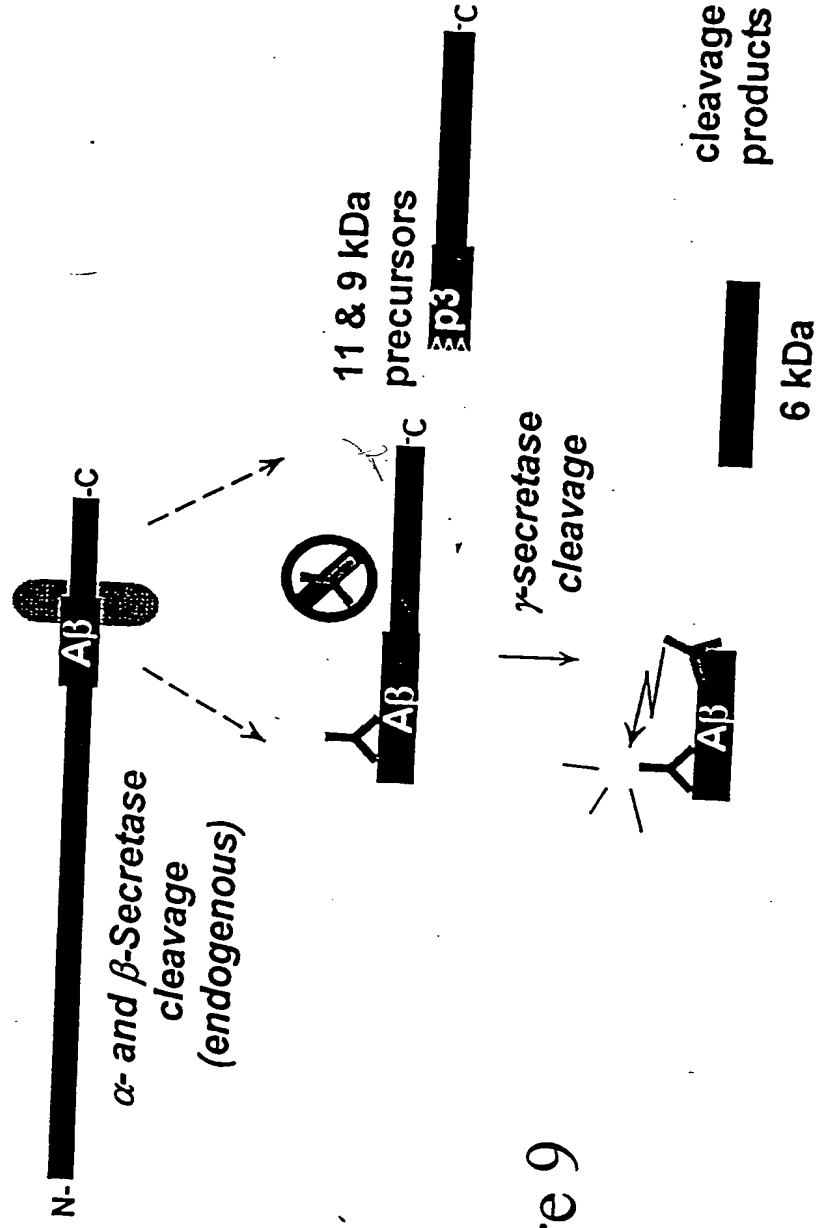


Figure 9

Membrane Titration

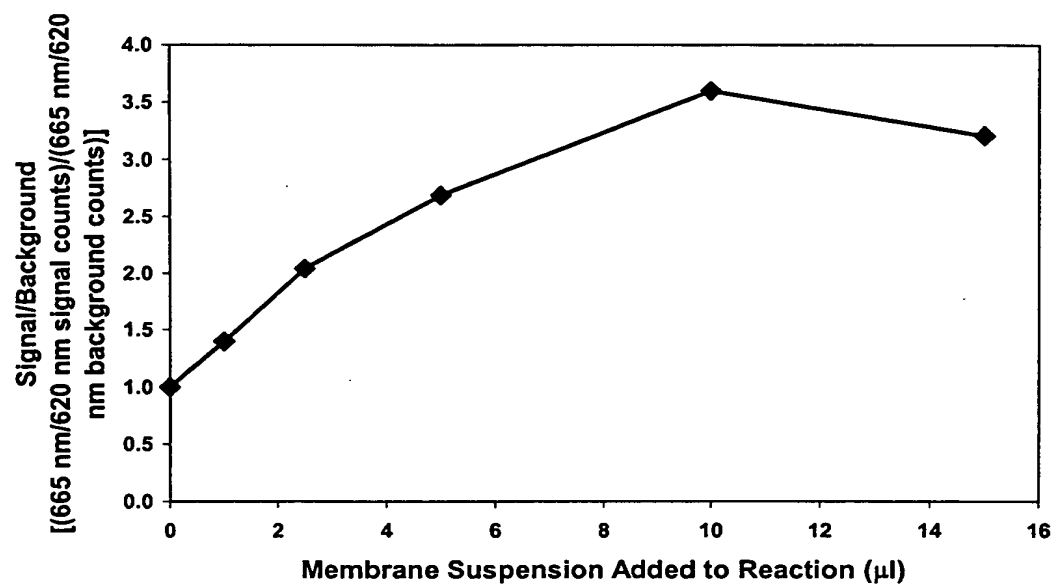


FIGURE 10

Detection of A β peptide by HTRF

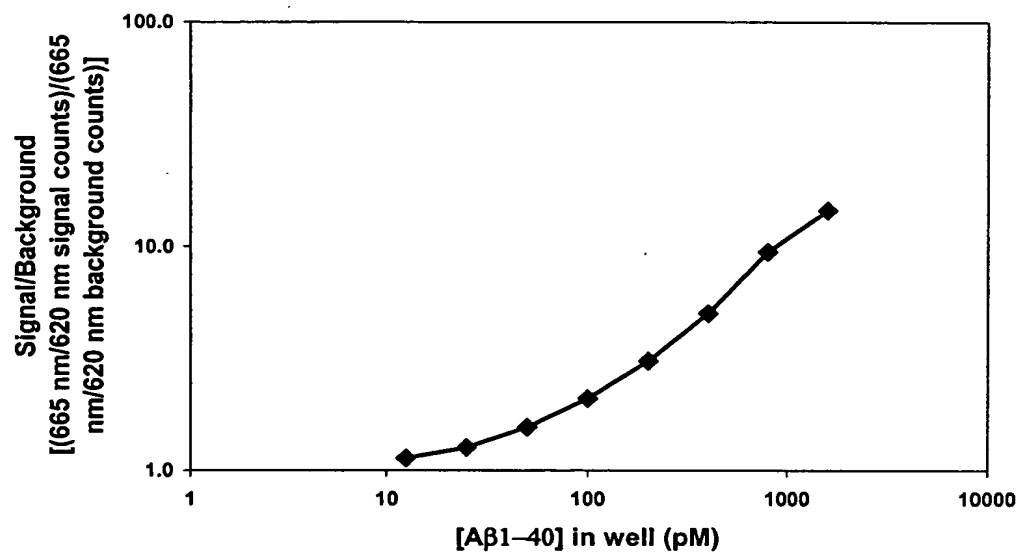
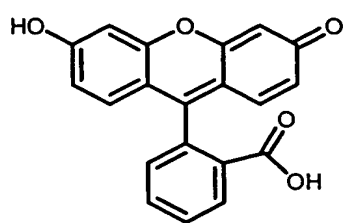
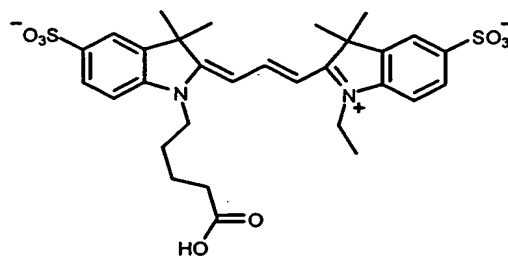


FIGURE 11

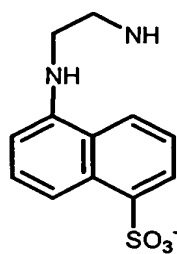
Fluorescent Donor Molecules



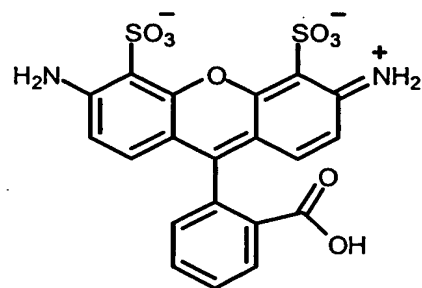
Fluorescein



Cy3



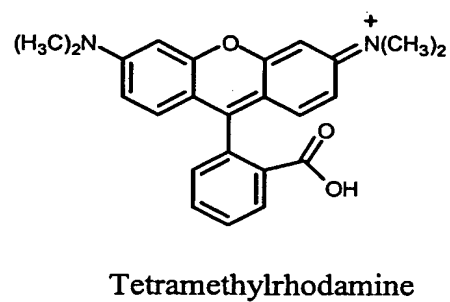
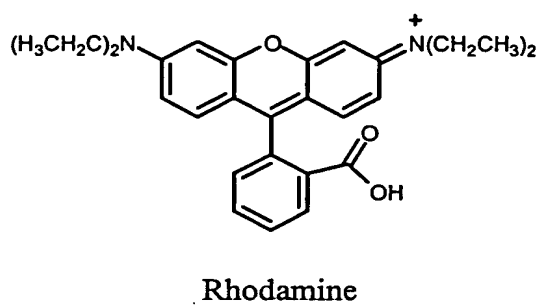
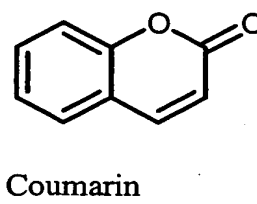
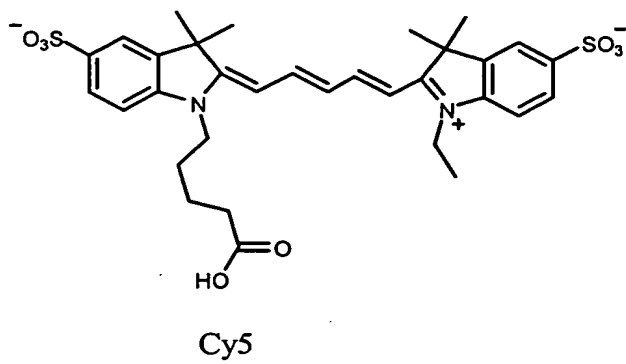
EDANS



Alexa Fluor

FIGURE 12

Fluorescent Acceptor Molecules



Fluorescent Acceptor Molecules which may act as Quenchers

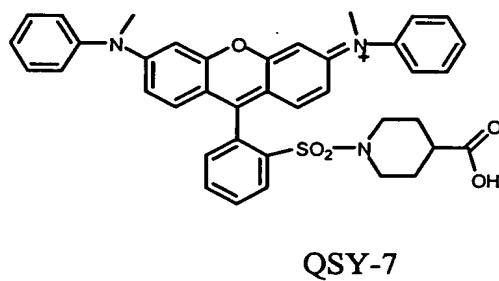
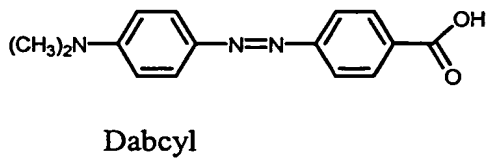


FIGURE 13